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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/705,519

11/10/2003

James M. Robl

50195/023003

4828

21559

7590

12/01/2006

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

CROUCH, DEBORAH

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/705,519

Applicant(s)

ROBL ET AL.

Examiner

Deborah Crouch, Ph.D.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 7-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 25-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 9/15/06.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Art Unit: 1632

Applicant's arguments filed September 15, 2006 have been fully considered but they are not persuasive. The amendment has been entered. The declarations filed under 35 U.S.C. § 1.132 by Dr. Yoshimi Kuroiwa have been considered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 25-38 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the office action mailed June 12, 2006. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are to a bovine comprising a non-naturally occurring mutation at one or both alleles of an endogenous prion nucleic acid, where the mutation is an insertion of a positive selection marker into a prion nucleic acid, bovine cells, methods of producing the transgenic bovine having reduced expression function prion protein.

Applicant argues declarant Kuroiwa states the specification provides ample guidance for one skilled in the art to product hemizygous and homozygous PrP knockout cells and bovines reproducibly. Applicant argues the specification teaches the production of a STOP sequence vector for disruption of the endogenous bovine PrP gene. Applicant argues that declarant Kuroiwa states bovine fibroblast line 6594 was transfected with pBPrP(H)Koneo and pBPrP(H)kOpuro vectors. Calves were obtained from fetal cell lines 5211, 5232 and 4296. Applicant argues declarant Kuroiwa states the health of the clone calves showed no abnormalities. These arguments are not persuasive.

Art Unit: 1632

The declaration is not clear as to the vectors used in the production of the calves taught in the declaration. The declaration does not teach the presence of a STOP codon/sequence in the vector to produce the cloned calves disclosed therein. Further, the cell lines transfected in the declaration are different from those used in the specification. The specification (page 60, Table 1) lists different cell line ID's in disclosing pregnancies established with the various PrPKO clones from those of the declaration (Kuroiwa, page 3). It is not possible to know from the declaration if the different vectors and different cell lines provided materials critical to production of cloned PrP KO bovines. That is to say, it is not possible to know if the particular cell lines used to produce the bovines of the declaration were critical.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 25-32 and 35-38 remain rejected under 35 U.S.C. 102(e) as being clearly anticipated by US 2002/0069423 (Good) for reasons set forth in the office action mailed June 12, 2006.

Good teaches heterozygous and homozygous bovines comprising an insertion of a positive selection marker into one or both alleles of an endogenous prion gene, where the bovines lack functional prion protein (page 6, parag. 0052, lines 1-4, page 18, parag. 00196 and page 19, parag. 0208).

Art Unit: 1632

Good also teaches a bovine fetal fibroblast comprising an insertion of a positive selection marker into one or both alleles of an endogenous prion protein gene, where function prion protein is not expressed (page 7, parag. 0074, lines 1-3; page 8, parag. 0091; page 9, parag. 0097, lines 16-20; and page 16, parag. 0165-0169).

Good teaches a method for producing a transgenic bovine cell having reduced expression of function prion protein comprising introducing into a first prion gene the insertion of positive selection marker targeting vector into a bovine fetal fibroblast under conditions that allow homologous recombination to produce a fibroblast having a hemizygous mutation and a homozygous mutation (page 16, parag. 0164-0167).

Good teaches the production of a transgenic bovine having reduced expression of functional prion protein comprising inserting a fetal fibroblast cell or its nucleus into an enucleated oocyte, wherein said cell comprises an insertion of a positive selection marker into a prion protein allele, transferring the oocyte to a surrogate mother and permitting term development (page 18, parag. 0184-0196).

Applicant has filed a declaration stating essentially that Good is not enabling. Applicant argues Good tried and failed to produce hemizygous prion protein knockout cell. Applicant argues Good failed to produce any experimental evidence that the methods described were operative. Applicant argues Good provides a prophetic example for production of a prion protein knockout. Applicant argues the distinction between Good and instant application is that the present application allows one of skill in the art to produce the inventions instantly claimed. These arguments are not persuasive.

Where the affidavit or declaration presented asserts that the reference relied upon is inoperative, the claims represented by applicant must distinguish from the alleged inoperative reference disclosure. In re Crosby, 157 F.2d 198, 71 USPQ 73 (CCPA

Art Unit: 1632

1946). Applicant has not distinguished the present claims from the disclosure of Good, nor has applicant explained what methodology they used provided PrP KO calves. Further, Good is U.S. Patent application and with a proper date for a 102(e). The proper course of action is to request an interference proceeding to establish the first to invent.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1632

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

November 24, 2006